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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,906	10/21/2005	Tomas Bergman	ALBI-41348	1877

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EXAMINER
WALICKA, MALGORZATA A

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,906	BERGMAN ET AL.	
	Examiner	Art Unit	
	MALGORZATA A. WALICKA	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *1-14 and 16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15 and 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/21/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence alignment entitled Nature 2001*.

Response to Restriction filed Feb 13, '08, is acknowledged. Claim 15 has been elected; new claims 21-23 have been added. Claims 1-23 are pending; elected claims 15, and 21-23 are under examination. Claims 1-14 and 16-20 are withdrawn from examiner's consideration as directed to a nonelected invention.

DETAILED ACTION

Election/restriction

Applicants elected Group II drawn to a method of treating colon cancer comprising administering a composition comprising Alk-Smase of SEQ ID NO: 1 and 4, and their variants, with traverse. The traverse is on the ground that

> "37 CFR 1.475, recited by the Examiner as not providing for multiple methods within a single application, merely states that failure to match the recited categories indicates that unity of invention "might not be present," not that it is definitively absent. Accordingly, Applicants respectfully request that the requirement for restriction of the claims be withdrawn."

Applicants' position has been carefully considered but is found not persuasive for the following reasons.

Applicants disclose two enzymes having different structures, but the same activity, and their encoding DNA. Groups I and III-IV have a special technical feature that is SEQ ID NO: 1. SEQ ID NO: 4 is not a contribution over the art because it was disclosed in The Journal of Biological Chemistry, 2003, 40, 38528-38536, as indicated in ISR. Nevertheless, the examiner, per examiner discretion, in order to speed up the prosecution of the whole disclosure and lower the prosecution costs, included both enzymes in groups I, III and IV. As to Group II, it does not comprise the same special technical feature because it is not directed to isolating the product identified by SEQ ID NO: 1 and 4 and furthermore is not a contribution over prior art because, the isolation of Alk-Smase is disclosed in article by Rui-Dong Duan

et al, Purification, localization, an expression of human intestinal alkaline sphingomyelinase, Journal of Lipid Res. 2003, 44, 1241-1250; quoted in the ISR.

Regarding Groups II-IV, they are directed to three methods different than the method incorporated in Group I. 37 CFR 1.475 does not provide for multiple products or methods within a single application and the methods are recognized in the art as completely different: enzyme isolation, enzyme therapy and gene therapy.

Thus, this restriction issued Nov. 29, 2007 was in applicants favor.

In the instant action the examiner, per her discretion, included to the elected group II, claims 21-23 directed to any method of enzyme therapy by SEQ ID NO: 1 and 4, including treatment of inflammation. These claims substantially broader the scope of the examined claimed invention.

In conclusion, the new group II includes claim 15, and 21-23. Other groups are as presented in the restriction requirement of Nov. 29/2007. This restriction is proper and MADE FINAL.

Rejections

35 USC 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 provides for the use of the polypeptide of SEQ ID NO:1 and 4 , their variants having at least 80% identity and alkaline sphingomyelinase comprising SEQ ID NO:3, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 21 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153

USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 22 and 23 are objected to as depending upon the rejected claim.

35 USC 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written description

Claims 15 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a genus of methods using a large genus of proteins hydrolyzing sphingomyelin wherein the structure of the proteins is not sufficiently described. The disclosure teaches human polypeptides SEQ ID NO: 1 and 4 that are two representatives of the genus of proteins that are used in the claimed methods. SEQ ID NO: 1 and 4 having definite structure and function but do not provide written description for:

1) any variant of SEQ ID NO: 1 having at least 80% identity with SEQ ID NO: 1,

2) any variant of SEQ ID NO: 4 having at least 80% identity with SEQ ID NO: 1, and

3) any isolated Alk –Smase comprising SEQ ID NO: 3 consisting of 18 amino acids.

Limitations “at least 80% identity with SEQ ID NO: 1”, “at least 80% identity with SEQ ID NO: 4”, and “comprising SEQ ID NO: 3” are partial recitations of structure. SEQ ID NO: 3 is part of SEQ ID NO: 1

(amino acids 70-87) and SEQ ID NO: 4 (amino acid 70-87). SEQ ID NO : 3 consists therefore of 4.26% of SEQ ID NO: 1 (422 amino acid long) and 3.9% of SEQ ID NO : 4 (458 amino acid long). The specification does not provide drawings or structural formulas for sequences having the required function and 80% identity to SEQ ID NO: 1 or 4. Neither SEQ ID NO: 3 can identify a protein having alkaline sphingomyelase activity. Thus the disclosure is lacking a description of how to make the polypeptides to be used in the claimed method. In addition, the state of art at the time of invention does not teach the structure-function relationship for the enzyme alkaline sphingomyelinase. Although a sequence being 80% identical to SEQ ID NO:1 was known, it was not annotated as sphingomyelinase; see the enclosed sequence alignment with mouse polypeptide; Nature 2001.

Claims 21 and 23 are rejected as containing new matter. The disclosure and the original claims do not teach that the enzyme may be administered to patients for any reasons; neither the disclosure teaches that the enzyme may be used for treating any kind of inflammation. What applicants disclose is inhibiting in vitro growth of human colon cancer cells. The method of inhibiting in vitro growth of human colon cancer cells does not identify any methods of treatment of patient or treatment of any inflammation as required by the claims.

In conclusion, one having skills in the art is not convinced that applicants were in possession of the claimed invention at the time the application was filed.

Scope of enablement

Claims 15 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a alkaline sphingomielinase of SEQ ID NO: 1 and 4, and their method of use, does not reasonably provide enablement for using any variant of SEQ ID NO: 1 and 4 being at least 80% identical to SEQ ID NO: 1 or 4, or any sphingomyelase comprising SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the claim must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)), otherwise, making and/or using the invention requires additional experimentation.

The factors to be considered in determining whether undue experimentation is required to make the invention are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are

(a) the quantity of experimentation necessary,

(b) the amount of direction or guidance presented,

(c) the presence or absence of working example,

(d) the nature of invention,

(e) the state of the prior art,

(f) the relative skill of those in the art,

(g) the predictability or unpredictability of the art, and the breadth of the claim.

The nature of the invention is using polypeptide of SEQ ID NO; 1 or 4, any of their variants having 80% identity and an activity of sphingomyelinase comprising SEQ ID NO: 3, wherein the enzyme is from any natural or human made source. Providing SEQ ID NO: 1 and 4 and the active center of SEQ ID NO: 3 is not a sufficient guidance as to the structure of the polypeptides being 80% identical to SEQ ID NO: 3 and 4; see the above rejection for lack of written description. Applicants do not teach which changes in amino acid sequences are neutral from the point of view of the activity of the polypeptide. 80% identity requires changes of almost 100 amino acids in primary sequences, which leads to and astronomical number of polypeptides to be tested: [485! x 19^{20}]/[485-97)!x97!]--even if the catalytic center of SEQ ID NO: 3 will not be changed. Although the skills of artisans in the field of protein mutagenesis are high, the unpredictability of obtaining active mutant is low, because the enzymes were not well known before the invention. Altogether, while enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that the claimed species have the functionality of Alk-Smase. The provision of SEQ ID NO: 1 or 4 fails to provide such guidance of

polypeptides with major structural variations therefrom which remain encompassed within the scope of the rejected claims.

In summary, without a further guidance on the part of Applicants regarding the structure of the polypeptides to be used in the claimed methods, experimentation left to those in the art is improperly extensive and undue.

Secondly, claims 21 and 23 are rejected because the specification, while being enabling for a alkaline sphingomyelinase of SEQ ID NO: 1 and 4, and their method of use for treatment of colon cancer, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, because they are directed to

1) any treatment of a patient with ESQ. ID NO: 1, 4 and their variants, and any Alk-Smase having SEQ ID NO: 3

2) treatment of any inflammation with SEQ ID NO: 1 and, 4 and their variants.

As to point 1, the claims are so broad as to include treatment, for any reasons, i.e. any disease. Thus, a skilled artisan would not know which one of thousands of conditions known in clinic to chose. Therefore, the experimentation imposed on the skilled artisan is having a very low probability of success without a teaching on the part of Applicants as to what conditions of a patient is suitable for treatment with Alk-Smase. Providing an example in which Alk-Smase inhibits colon cancer cell in vitro is not a sufficient guidance for treating any condition. In summary, one having skills in the art is forced to experimentation that is undue.

Regarding point 2), although the scope of claim 23 is narrower than that of claim 21, inflammations have different underlying mechanisms, and not every inflammation can be treated with Alk-Smase. Applicants suggest that bowel inflammation preceeding carcinogenesis is related to insufficient production of Alk-Smase; any experimental daa are provided to support this suggestion. Also, other inflammations are not shown to depend on the enzyme. In conclusion, without a further teaching on the part of applicants as to the kind of inflammation to be treated by Alk-Smase, one having skills in the art, who

would like to make and use the claimed invention, is forced to experimentation with a low probability of success and undue.

Conclusion

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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